be found in the specification at page 5, lines 35-38, at page 6, lines 24-25, and at page 7, lines 9-12. Support for claims 88-93 may be found in the specification at page 3, lines 28-35. Further support for claims 47, 77 and 91 may be found in the specification at page 4, lines 5-10. No matter has been added.

For the avoidance of doubt, Applicants note that, as set forth in the specification, "5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione" (or "Compound (I)") may exist in one of several tautomeric forms, as individual tautomeric forms or as mixtures thereof, all of which are encompassed by the term "Compound (I)" or "5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione". Furthermore, 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione contains a chiral atom, and therefore can exist in up to two stereoisomeric forms. The term "5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione" (or "Compound (I)") also encompasses all of these isomeric forms, whether as individual isomers or as mixtures of isomers, including racemates. See the specification at page 4, lines 11-15. Accordingly, when reference is made to "Compound (I)", or to "5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione", or to "5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, or a tautomer thereof", or to "said 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione ", all tautomeric and isomeric forms of the compound are intended to be encompassed.

Additionally for the avoidance of doubt, as set forth in the specification, when reference is made to scalar amounts, including mg amounts and % weight amounts, of "5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione in a pharmaceutically acceptable form" (or as in the claims: "said 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione in a pharmaceutically acceptable form"), the scalar amount referred to is made in respect of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione per se: for example, 2 mg of Compound (I), or 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, in the form of the maleate salt is that amount of maleate salt which contains 2 mg of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (not: 2 mg of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione maleate salt). See the specification, page 5, lines 3-7.

Although no official action has been taken regarding claims 23-93, these claims define the same subject matter and contain many of the same terms as original claims 1-22 that were examined and were the subject of the Office Action dated November 20, 2002. To expedite prosecution of the subject application, Applicants will address the objections raised in the Office Action to the extent that they pertain to the claims. Original claims 1-22 had been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Applicants' admissions at page 1, lines 3-38 of the subject specification ("the Background discussion"). Applicants respectfully traverse the rejection in the Office Action.

The Examiner rejected original claims 1-22 , contending that it would have been *prima facie* obvious to administer co-jointly insulin and compound of claims 1-13 to treat diabetes with the compositions of claim 14-22.. As an initial mater, Applicants respectfully submit that, although insulin may be used in the methods and compositions of the present invention, insulin is not a recited element in either original claim 1 or in any of the new independent claims 23, 53, or 83-87. Accordingly, contrary to the Examiner's assertion, insulin is not a necessary element of the present invention. Applicants will address the Examiner's objection form the perspective of using the recited combination of insulin sensitizer, insulin secretagogue and biguanide. In this regard, Applicants respectfully submit that the Examiner's objection fails to recognize the specificity of the dosing ranges of Compound (I) as defined in original claims 4-12.

It is well settled that to establish a *prime facie* case of obviousness, there must be 1) some motivation to modify the cited reference, 2) a reasonable expectation of success, and 3) the prior art reference must teach or suggest all the claim limitations.

To expedite prosecution of the subject application, Applicants have presented new claims that are limited to the use of 2-12 mg per day of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione with glimepiride and metformin. Applicants respectfully submit that the Background discussion, or the art cited therein, fails to disclose or provide any suggestion to use Compound (I), glimepiride and metformin in the specifically recited amounts as provided in new claims 23-93 to treat diabetes mellitus and conditions associated therewith, particularly Type II diabetes.

Applicants respectfully submit that the Background discussion fails to support a *prime facie* case of obviousness by:

1) failing to provide any motivation to select the claimed dosages of Compound (I) to be used in combination with glimepiride and metformin to treat diabetes mellitus and conditions associated therewith, specifically Type II diabetes;

2) failing to provide any guidance or a basis for expectation of success that Compound (I) can be used, in combination with glimepiride and metformin, in the amount of 2 to 12 mg per day to treat diabetes mellitus and conditions associated therewith, specifically Type II diabetes;

3) failing to disclose or suggest that Compound (I) can be used in the amount of 2 to 12 mg per day, in combination with glimepiride and metformin, to treat diabetes mellitus and conditions associated therewith, specifically Type II diabetes; and

4) failing to disclose or suggest administering Compound (I) one to two times per day in a unit dosage form of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 mg, in combination with glimepiride and metformin, to treat diabetes mellitus and conditions associated therewith, specifically Type II diabetes.

Assuming *arguendo*, that it would have been obvious to try to treat diabetes mellitus and conditions associated therewith in patients using Compound (I) in combination with an insulin secretagogue and a biguanide, the Background discussion fails to disclose or suggest that patients can be effectively treated using the specific combination of Compound (I), glimepiride and metformin, wherein Compound (I) is used in the amount of 2 to 12 mg per day, specifically by administering Compound (I) one to two times per day in a unit dosage form of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 mg. Obvious to try or experiment is not the standard under §103.

Applicants respectfully submit that the Background discussion fails to disclose or provide any suggestion to use the specifically recited components and to use them in the specifically recited amounts as provided in new claims 23-93.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the presently claimed invention is patentable over the Background discussion at page 1, lines 6-18 of the subject specification and that subject application is in condition for allowance. If the Examiner has any remaining objections or concerns, the Examiner is respectfully requested to contact

Applicants' undersigned attorney to resolve such issues and advance the case to issue.

INFORMATION DISCLOSURE STATEMENT

In compliance with the duty of disclosure under 37 C.F.R. §1.56, and in accordance with the practice under 37 C.F.R. §1.97, the Examiner's attention is directed to the documents listed on the enclosed Form PTO 1449. A copy of each of the listed documents is also enclosed. The filing of this Information Disclosure Statement should not be construed as an admission that any particular listed reference is effective prior art or discloses or renders obvious any aspect of the claimed invention.

This statement is being filed under the provisions of 37 C.F.R. §1.97(c)(2), before the mailing date of a Final Office action or before the mailing date of a Notice of Allowance. Please charge the $180.00 fee specified in 37 C.F.R. §1.17(p) to the Deposit Account No. 19-2570.

It is respectfully requested that the above information be considered by the Examiner and that a copy of the enclosed Form PTO-1449 be returned indicating that such information has been considered.

This Amendment and Information Disclosure Statement is being filed together with Petition for Extension of Time. In the event that these papers get separated, this constitutes a Petition for Extension of Time for the minimum period required to effect timely filing of this Amendment and Information Disclosure Statement, together with an authorization to charge any fees under 37 C.F.R. §1.16 or §1.17 which may be required by this paper to Deposit Account No. 19-2570.

Respectfully submitted,

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